Trend Watch

CURRENT MANAGEMENT OF SCHIZOPHRENIA: Antipsychotic Monotherapy versus Combination Therapy

by Elisa F. Cascade; Amir H. Kalali, MD; Peter F. Buckley, MD

AUTHOR AFFILIATIONS: Ms. Cascade is Vice President, Quintiles Inc./iGuard, Falls Church, Virginia; Dr. Kalali is Vice President, Global Therapeutic Group Leader CNS, Quintiles Inc., San Diego, California, and Professor of Psychiatry, University of California, San Diego; and Dr. Buckley is Professor and Chairman, Department of Psychiatry, Medical College of Georgia, Augusta, Georgia.

ADDRESS CORRESPONDENCE TO: Ms. Elisa Cascade, Vice President, Quintiles, Inc.,/iGuard, 3130 Fairview Park Drive, Suite 501, Falls Church, VA 22042; E-mail: elisa.cascade@quintiles.com

FINANCIAL DISCLOSURES: Dr. Buckley has received grant/research support from AstraZeneca, National Institute of Mental Health, Pfizer, Solvay, and Wyeth, is a consultant to AstraZeneca, Bristol Myers Squibb, Eli Lilly, Janssen Pharmaceutica, Lundbeck, Pfizer, Solvay, and Wyeth, and has received honorarium/expenses from Bristol Myers Squibb, Janssen Pharmaceutica, Lundbeck, and Pfizer.

ABSTRACT: We investigated the current practice for treatment of schizophrenia. According to our data, 47 percent of patients with schizophrenia are treated with only antipsychotic medication. An additional 43 percent of patients receive one additional class to supplement their antipsychotic medication, and 10 percent of patients are prescribed two or more classes of drugs in addition to an antipsychotic medication. The most common classes used to supplement antipsychotic medications in the management of schizophrenia include antidepressants (28%), mood stabilizers (18%), agents to treat extrapyramidal symptoms (7%), and sleep aids (5%).

KEY WORDS: schizophrenia, monotherapy, combination therapy, augmentation, antipsychotics, antidepressants

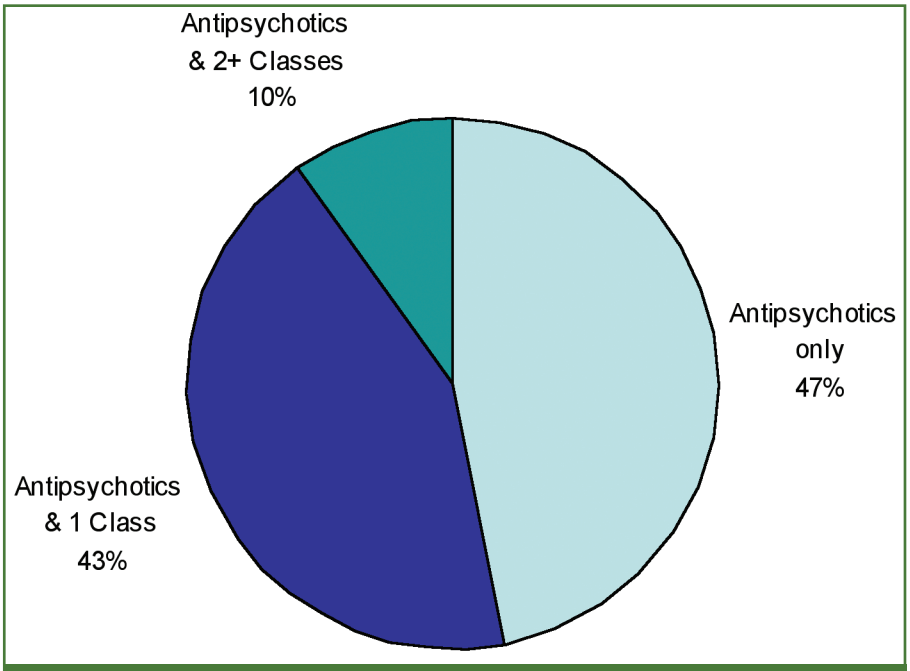

FIGURE 1. Treatment of schizophrenia
Source: Verispan PDDA, ICD-9 Diagnosis 295, March 2007 to February 2008.

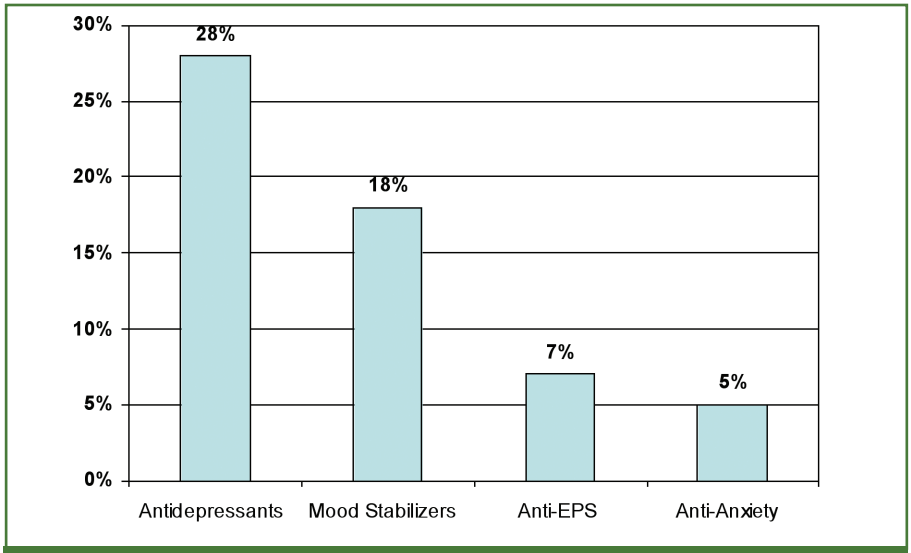

FIGURE 2. Products used in combination with antipsychotics for schizophrenia treatment
Mood stabilizers include antiepileptics and lithium.
Source: Verispan PDDA, ICD-9 Diagnosis 295, March 2007 to February 2008.

INTRODUCTION

To better understand current practice for the management of schizophrenia, we investigated the use of antipsychotics alone and the need for supplementation with other classes of agents to control symptoms.

METHODS

We obtained data on product treatment regimen from Verispan's Prescription Drug and Diagnosis Audit (PDDA) database from March, 2007, to February, 2008, for schizophrenia as defined by ICD-9 diagnosis code 295. PDDA captures data on disease state and associated therapy from 3,100 office-based physicians representing 29 specialties across the United States.

RESULTS

As seen in Figure 1, 47 percent of patients with schizophrenia are treated with only antipsychotic medication. An additional 43 percent of patients receive one additional class to supplement their antipsychotic medication, and 10 percent of patients are prescribed two or more classes of drugs in addition to an antipsychotic. According to our data, 28 percent of patients with schizophrenia are prescribed an antidepressant in combination with their antipsychotic (Figure 2). Other therapeutic classes used to supplement antipsychotics in the management of schizophrenia include mood stabilizers (including lithium or antiepileptics, 18%), agents to treat extrapyramidal symptoms (7%), and sleep aids (5%).

COMMENTARY

by Peter Buckley, MD

These data, drawn from clinical practice-prescription profile analyses, "jive well" with what is currently happening in our clinics and in our hospitals. The treatment of schizophrenia and bipolar disorder have (paradoxically) become increasingly complex with the greater availability and choice among antipsychotic medications. At the same time, there is still a

substantial unmet need, as confirmed by recent, large, pragmatic trials in schizophrenia and bipolar disorder, that provides the therapeutic context for antipsychotic polypharmacy as well as the use of other psychotropic medications alongside antipsychotics. For patients and clinicians, then, the question of "why and when do I combine medications?" is now very challenging. As these data also bear out, other available evidence suggests that antipsychotic polypharmacy is common in clinical practice. Additionally, it is a topic of enduring interest among clinicians who are always eager to understand the information contributing to key therapeutic strategies. These data also attest to the high rates of concomitant use of other psychotropic agents, particularly antidepressant medications.

At the present time, we are lacking robust research literature to guide this decision-making process that is the clinician's dilemma: Why, when, and how should I use antipsychotic polypharmacy to its best advantage in my practice? Available scientific evidence for polypharmacy strategies in schizophrenia is scant and does not preferentially endorse any single strategy. This latter point is particularly relevant when proponents of polypharmacy say "Hey, this approach works for my patients" yet cannot articulate a single drug option, and so it again resides in the individualization of care for patients with schizophrenia. Another consideration to bear in mind here is that some polypharmacy is not so much driven by augmentation strategies, but rather by "suspended" switching strategies. That is, you and your patient decide to switch medications but you ended up stopping this midway, and so the patient stays on both medications...and ends up in the so called *psychopharmacological purguratory* as Dr. Peter Weiden has aptly termed this.

Available scientific evidence for polypharmacy strategies in schizophrenia is scant and does not preferentially endorse any single strategy. This latter point is particularly relevant when proponents of polypharmacy say "Hey, this approach works for my patients" yet cannot articulate a single drug option, and so it again resides in the individualization of care for patients with schizophrenia.

The sizeable rate of concomitant use of antidepressants recorded in these analyses is also worthy of comment. It is well known that patients with schizophrenia get depressed. Depression in schizophrenia worsens the outcome, both in terms of heightening the risk of psychotic relapses and also greatly increasing the risk of suicide. Accordingly, the prescription of antidepressant medications for patients with schizophrenia who become depressed is an important therapeutic strategy. Interestingly, recent work on antidepressant therapy for mood disorders suggests that these drugs may have neuroprotective effects, perhaps through increasing the brain's neurotrophins, such as brain-derived neurotrophic factor (BDNF). Interestingly, the clinical and translational impact of antidepressant therapy has not yet been studied in the context of second generation antipsychotic medications (beyond clozapine). These data would suggest that clinicians are using these agents regularly in the treatment of patients with schizophrenia.

It would be useful to have some data from pragmatic trials to inform this fundamental practice strategy for clinicians and to examine the extent to which polypharmacy truly impacts both efficacy and tolerability considerations in treating patients with schizophrenia.